

Application No. 09/780,646

Applicant: Hubert DORN, et al.

Amendment in Reply to Office Action of March 27, 2003

**CONDITIONAL PETITION FOR EXTENSION OF TIME**

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefor. The Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

**ADDITIONAL FEE**

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

**REMARKS/ARGUMENTS**

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

At the outset, Applicants wish to clear up some confusion, which, in retrospect, appears to be caused by the wording of main claim 10. Applicants believe that persons skilled in the art will clearly understand what was intended. However, the Examiner's comments lead Applicants to believe that they may have confused the Examiner. If so, then, hopefully, the following discussion, coupled with the amendments to claim 10, will clear the confusion.

The word "non-systemic" in the instant claims refers to the application and action on the host animal. In other words, the application of the compound to the host human or animal should

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not result in the compound becoming systemically distributed within the host. Applicants found, for example, that the compounds of formulae (II) and (III) have a surprisingly good long-term activity when applied topically to an animal. In practice this is done with so called spot-on formulations which means that a small amount (e.g. 1 or 2 ml) of a liquid formulation are applied to the back of e.g. a dog. The formulation then spreads over the animal and offers complete protection against parasitic insects (e.g. fleas) for a period of about four weeks. From Applicants' experiments, it is known that the active compounds remain on the surface of the animal and act on the fleas by contact. Obviously the mode of action in the fleas is "systemic."

It is also possible to administer neonicoinoid compounds (a more general term for the active ingredients used in the method claimed in the present patent family) systemically, usually by oral application. In this case, the active ingredient is distributed in the blood circulation and the fleas incorporate the active ingredient during their blood meal. However, this application route has the disadvantage that the active ingredients are quite rapidly metabolized and as a consequence the ectoparasiticidal activity decreases within a comparatively short term. In other words, the systemic route typically does not provide long-term activity.

Evidence can be found in the Hansen Declaration, of record, where the non-systemic spot-on application is compared to the systemic oral application. In particular, the data on page 10 shows that the long-term activity upon spot-on application (non-systemic) is by far better than upon oral application (systemic).

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Consequently, according to the teachings of the present invention, it is desirable to minimize any penetration through the skin into the blood circulation of the host because – as explained above – this would lower the long-term activity.

To make the wording of claim 10 clearer, “non-systemically” has been deleted from the preamble, and a “wherein” clause has been added at the end. The “wherein clause simply states the meaning of “non-systemic,” i.e., the contacting does not result in the compound being systemically distributed within the human or animal host. Inasmuch as the “wherein” clause simply states the meaning of “non-systemic,” as it would be clear to any person skilled in the art reading the instant specification, Applicants submit it does not introduce new matter.

Claims 10-15 were rejected under 35 U.S.C. § 112, first paragraph, as being broader than the enabling disclosure. In response, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

The data provided in the Hansen Declaration, of record, has been explained above. Again, it provides a comparison of non-systemic and systemic applications to the host. Again, the data shows that long-term activity upon spot-on application (non-systemic application to the host) is by far better than oral application (systemic application to the host.) The effects to the fleas are systemic to them. However, as noted above, claim 10 is clarified to make clear that

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non-systemic effects on the host, i.e., the human or animal, is what is at issue.

The Examiner takes the position that the specification does not enable persons skilled in the art to use the invention commensurate in scope with the claims. The Examiner says that not all compounds are capable of meeting the "not systemic" criteria, and still meeting efficacy for "control." The Examiner has not provided any support for this position in the form of sound scientific reasoning or evidence. Even if the Examiner's position were true, this does not cast any doubt on the enablement since the "wherein" clause of claim 10 limits the claims to only operative embodiments. In other words, claim 10 only covers embodiments wherein the compound can be contacted with the parasitic insect without the compound being systemically distributed within the host human or animal. Viewed in this light, it should be clear that the claims are tailored to be exactly commensurate in scope with the enablement.

The Examiner says only specific compounds are shown to be able to be applied at effective doses to "control" fleas without systemic effects via the host. However, these are only representative examples. The Examiner has not advanced any reason to believe that the claims embrace a significant content of inoperable subject matter. In point of fact, they do not because, as noted above, the "wherein" clause of claim 10 restricts the claims to operable embodiments only.

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Respectfully, the allegations in the specification must be accepted as true in the absence of reasonable doubts supported by sound technical reasoning or evidence. *In re Marzocchi et al.*, 169 USPQ 367, 369 (CCPA 1971). The Examiner has not provided any sound technical reasoning or evidence tending to cast doubt on the enablement. Consequently, the enablement must be accepted as true.

In view of the foregoing, Applicants submit that the Examiner would be fully justified to reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Claims 10-15 were rejected under 35 USC § 103(a) as being obvious over European Patent Application No. 0 285 985 ("EP-A-0 285 985") and European Patent Application No. 0 259 738 ("EP-A-0 259 738"). In response, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

The Examiner takes the position that the steps of the instant method are indistinguishable from those of the cited prior art. In response, Applicants submit that this is clearly no longer the case. As indicated above, claim 10 has been amended to include a "wherein" clause, which makes clear that as a result of the "contacting" the compound is not systemically distributed within the human or animal host. This is different from the prior art, which, as exemplified by WO 93/24002, of record, established that only systemic application is suitable for compounds of

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the type involved here. Thus, Applicants' discovery of the effectiveness of non-systemic application flies in the face of the prejudice against such application as clearly evident in the prior art. That Applicants proceeded in the face of the prior art, and accomplished the present invention, is evidence of an inventive contribution, which is, thus, deserving of patentability.

To reiterate, "dermal" is not synonymous with "non-systemic." It is well known in the art that many active substances, albeit they are dermally applied, may penetrate the skin, enter the bloodstream and be distributed throughout the body in a systemic manner. Thus, simply because a reference teaches dermal application does not necessarily mean that the application is also non-systemic.

The Examiner has not established the well known state of the prior art to be other than Applicants have set forth in the preceding paragraph. Therefore, the present rejection cannot be maintained simply by showing that the cited prior art mentions dermal application. Instead, the Examiner must show that the prior art teaches or suggests non-systemic application specifically. Applicants submit that the cited references nowhere teach or suggest non-systemic application specifically. Consequently, the Examiner should reconsider and withdraw this rejection.

To the best of Applicants' knowledge, at the time the present invention was made, persons skilled in the art would not have considered the non-systemic application of the compounds of the present claims in order to control ectoparasitic insects on animals or humans.

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Such persons also would not have expected their surprisingly high efficiency over a long-term.

While referring to a different type of compounds, *but of the same class of agonists or antagonists of the nicotinergic acetylcholine receptors of insects*, the introductory part of WO 93/24002, of record here, as noted above, accurately reflects the thinking of persons skilled in the art at the time the present invention was made. Although dermal application of active ingredients to animals was, of course, known in general principle, WO 93/24002, as noted above, discloses that only systemic application is suitable for the compounds disclosed therein. Thus, non-systemic application was clearly thought to be unsuitable for compounds such as are described in WO 93/24002.

The same expectation applied to the specific compounds required by the instant claims. The prevailing thought was that systemic application must be achieved, even if the application was a dermal application. Nothing in the cited references suggests otherwise.

EP-A-0 285 985 lists virtually all known application forms for veterinary medicine. See page 7, lines 31 ff, of the German text. However, as all of these application forms are listed without specific comments or preferences, the document does not surmount the prejudice in the art that systemic application must be achieved. Consequently, the reference would not have led persons skilled in the art to carry out dermal application in such a way as to achieve non-systemic application, as presently claimed.

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"Laundry lists," of the type set forth in EP-A-0 285 985, have been held in some instances not to constitute a written description of an embodiment sufficient to support an anticipation rejection under 35 USC § 102. *See, e.g., In re Wiggins et al.*, 179 USPQ 421, 425 (CCPA 1973).

In further support of Applicants' position, Applicants previous supplied a partial translation of the paragraphs of EP-A-0 285 985 upon which the Examiner relies. Although the reference does mention dermal application, the reference is silent as to the achievement of non-systemic control. Consequently, EP-A-0 285 985 would not, in fact, have suggested non-systemic application to persons skilled in the art.

With respect to EP-A-0 259 738, the Examiner previously pointed to page 9, lines 35-42. However, Applicants again point out that in line 36, the reference discloses that the compounds are active against *endoparasites*, such as worms. Although the reference also teaches usefulness against ectoparasites, the reference does not make a distinction between the methods to be used to treat endoparasites and those to be used to treat ectoparasites, and, thus, a person having ordinary skill in the art would have been led to the conclusion that the two methods are the same. Obviously, endoparasites, because they are inside of the host animal, must be treated by a method that brings the active compound into the body of the host animal, which method is necessarily a systemic method. Ectoparasites could also have been treated by the same systemic method. Consequently, EP-A-0 259 738 also would not have suggested non-systemic application to persons skilled in the art.

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To the extent that non-systemic dermal application is considered to be an obvious choice of administration method, Applicants would request that the Examiner reconsider the data of record. The data show that the results achieved with non-systemic dermal application are superior even to those obtained with oral treatment. There is absolutely nothing in the cited prior art that teaches or suggests the superiority of non-systemic dermal application over oral treatment. Consequently, the data in the declarations of record are proof of a surprising and unexpected result, which is, thus, objective evidence of nonobviousness.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

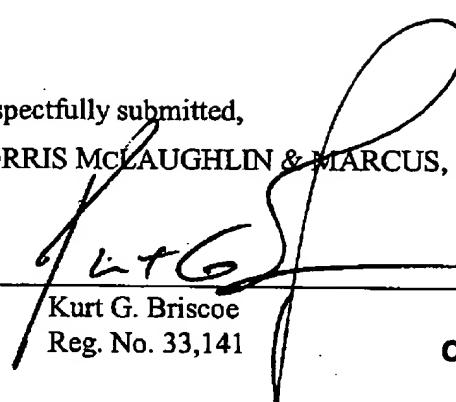
Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

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Early and favorable action is earnestly solicited.

Respectfully submitted,

NORRIS MC LAUGHLIN & MARCUS, P.A.

By 

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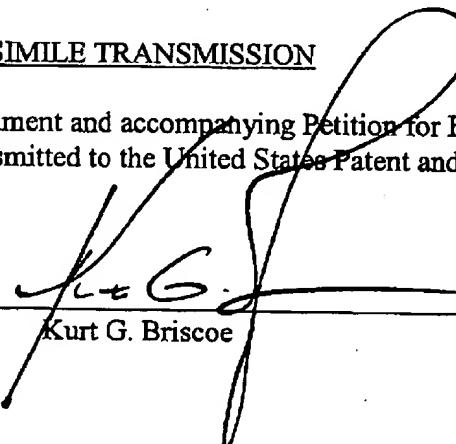
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OFFICIAL

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the foregoing Amendment and accompanying Petition for Extension of Time (15 pages total) are being facsimile transmitted to the United States Patent and Trademark Office on the date indicated below:

Date: September 29, 2003

By 

Kurt G. Briscoe